

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1-19. (cancelled)

20. (currently amended) [[An]] A positively charged  
oligomeric conjugate positively charged, comprising:

an oligomer with a polymerization degree (PD) from 5 to 36, formed from monomeric components comprising monomeric components having substituted  $\text{NH}_3^+$  and monomeric components having unsubstituted  $\text{NH}_3^+$ , wherein

a) ~~said monomeric component is substituted in a ratio of at least 50%~~ monomeric components having substituted  $\text{NH}_3^+$  represent at least 50% by monomeric components, said ratio being determined by nuclear magnetic resonance, by protonable residues, said residues being protonated in a weak acid medium, said protonation leading to a destabilization of a cellular membrane,

b) said protonable residues possess the following properties:

said protonable residues contain a functional group enabling them to be linked to said oligomer,

~~said protonable residues are not recognized as a recognition signal recognized by a cellular membrane receptor,~~

said protonable residues comprise at least one unsubstituted  $\text{NH}_3^+$  group selected from the group consisting of imidazoles, quinolines, pterines, and pyridines,

c) ~~[[the]]~~ where  $\text{NH}_3^+$  groups of said monomers are optionally substituted by uncharged residues leading to a reduction of the number of positive charges in comparison to the same oligomer before substitution,

d) molecules constituting a recognition signal recognized by a membrane cellular receptor are optionally present:

by substitution of some of the  $\text{NH}_3^+$  of said monomers,

on some of the uncharged residues leading to a reduction of the number of charges,

on some of said protonable residues leading to a destabilization of a cellular membrane, or

by substitution of the  $\text{NH}_3^+$  ~~(if it is present)~~ of said protonable residues, if said protonable residues are present, leading to a destabilization of a cellular membrane, provided that the total number of the non-substituted  $\text{NH}_3^+$  ~~functions~~ groups is of at least 50% of the polymerization degree.

21. (previously presented) The oligomeric conjugate according to claim 20, wherein the protonable residues leading

to a destabilization of cellular membranes have a pK in aqueous medium lower than 8.0.

22. (currently amended) The oligomeric conjugate complex according to claim 20, wherein said protonable residues are compounds selected from the group consisting of:

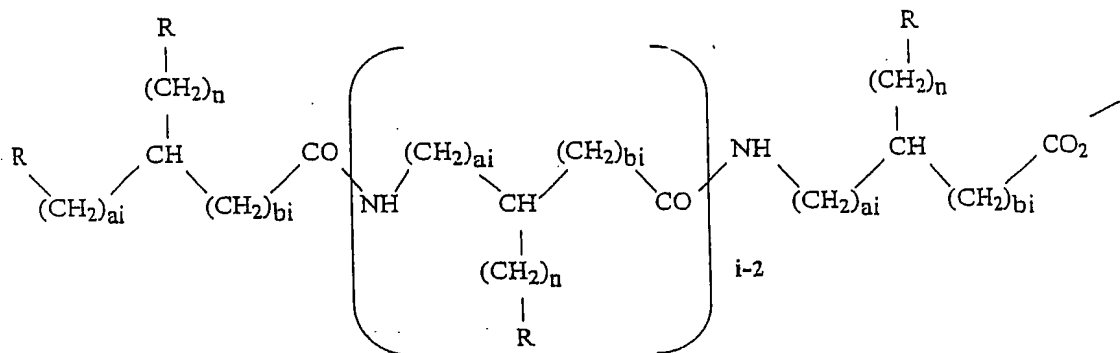
~~imidazoles,~~  
~~quinolines,~~  
pterines, and  
pyridines.

23. (previously presented) The oligomeric conjugate according to claim 20, wherein said protonable residues comprise alkyimidazoles in which the alkyl radical has from 1 to 10 carbon atoms, and only one nitrogen atom of the imidazole ring is substituted.

24. (currently amended) The oligomeric conjugate according to claim 20, wherein the protonable residues leading to a destabilization of cellular membranes are selected from the group consisting of histidine, 4-carboxymethyl-imidazole, 3-(1-methyl-imidazol-4yl)-alanine, 3-(3-methyl-imidazol-4yl)-alanine, 2-carboxy-imidazole, histamine, 3-(imidazol-4yl)-L-lactic acid, 2-(1-methyl-imidazol-4yl)ethylamine, 2-(3-[[metyl]]methyl-[[limidazol]]imidazol-4yl)ethylamine,  $\beta$ -alanyl-histidine-(carnosine), 7-chloro-4(amino-1-methylbutylamino)-quinoline, N4-(7-chloro-4-quinolinyl)-1,4-pentanediamine, 8-(4-amino-1-methylbutylamino)-6-methoxy-quinoline (primaquine), N4-(6-

methoxy-8-quinolinyl)1,4-pentanediamine, quininic acid, quinoline carboxylic acid, [[pteroid]] pteroic acid, nicotinic acid, and quinolinic acid.

25. (previously presented) An oligomeric conjugate having the following formula:



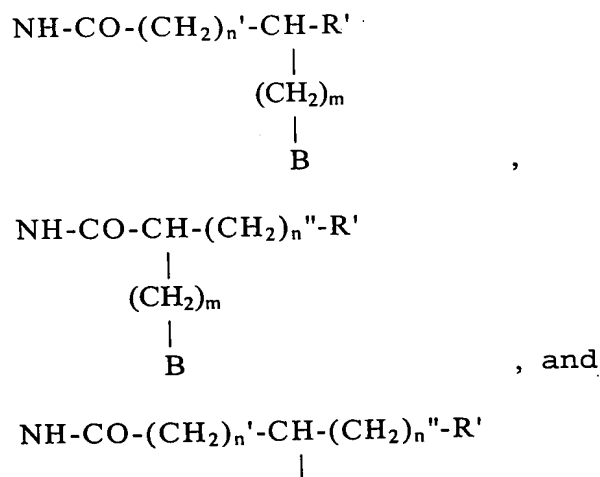
wherein:  $a_i$  = an integer varying from 0 to 10,

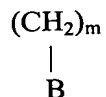
$b_i$  = an integer varying from 0 to 10,

$i$  = degree of polymerization from 5 to 36,

$n$  = an integer varying from 1 to 6,

wherein 50% to 100% of all R groups are selected from the group consisting of





wherein  $m$  = an integer varying from 1 to 6,

$n'$  = an integer varying from 0 to 6,

$n''$  = an integer varying from 0 to 6,

$B$  = a weak base,

$R'$  represents  $\text{NH}_3^+$  (corresponding to a number  $p$ );

or  $\text{NH}$  (corresponding to a number  $q$ ) substituted  
by a structure selected from the group consisting of

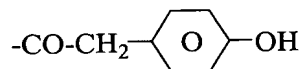
$-\text{CO}-\text{CH}_3,$

$-\text{CO}-(\text{CHOH})_r\text{H}$

$r$  being an integer from 1 to  
15,

$-\text{CO}-(\text{CH}_2)_s-(\text{CHOH})_r\text{H}$

$r$  being an integer from 1  
to 15, and  $s$  being an  
integer from 1 to 6,



$-\text{SO}_2\text{-Flu},$

$-\text{CO-Flu},$  and

$-\text{CS-NH-Flu}$

wherein  $\text{Flu}$  is a fluorescent molecule; and wherein

0% to 50% of all  $R$  groups (corresponding to  $f$

wherein:  $0 < f \leq u$ ) are

$\text{NH}_3^+$  (corresponding to a number  $j$ ); or

$\text{NH}$  (corresponding to a number  $k$ ), substituted by a

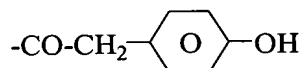
structure selected from the group consisting of

-CO-CH<sub>3</sub>,  
-CO-(CHOH)<sub>r</sub>H

r being an integer from  
1 to 15,

-CO-(CH<sub>2</sub>)<sub>s</sub>-(CHOH)<sub>r</sub>H

r being an integer from  
1 to 15, and s being an  
integer from 1 to 6,



-SO<sub>2</sub>-Flu,

-CO-Flu, and

-CS-NH-Flu wherein

Flu is a fluorescent molecule; or

H (corresponding to a number h); or

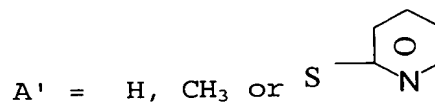
(CH<sub>2</sub>)<sub>n</sub>H

n being an integer from  
1 to 6 (corresponding  
to a number h); or

(CH<sub>2</sub>)<sub>n</sub>-OH

n being an integer from  
1 to 6 (corresponding to  
a number h); or

(CH<sub>2</sub>)<sub>n</sub>-SA'



n being integer from 1  
to 6 (corresponding to a  
number h)

with  $i = u + j + k + h$

total number of  $\alpha \text{ NH}_3^+ = p = u - q$

total number of  $\omega \text{ NH}_3^+ = j = f - (k + h)$

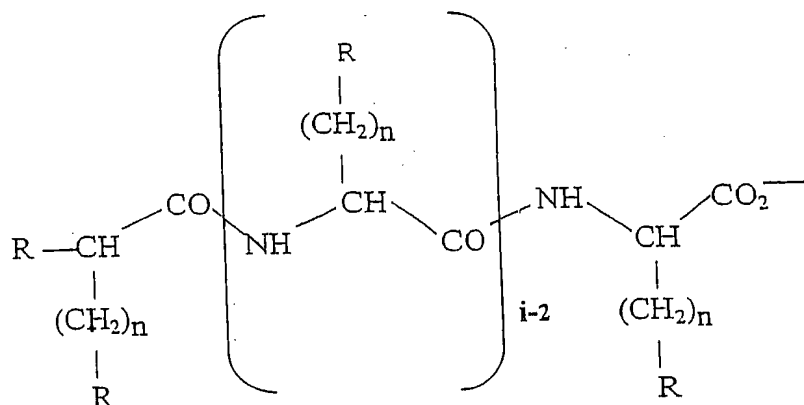
total number of  $\text{NH}_3^+ = m = p + j + 1$

with the proviso that:

1)  $u \geq i/2$

2)  $m \geq i/2$ .

26. (previously presented) The oligomeric conjugate according to claim 25, wherein the oligomeric conjugate contains an oligomer of the following formula:

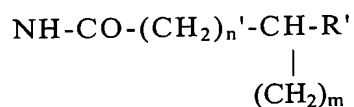


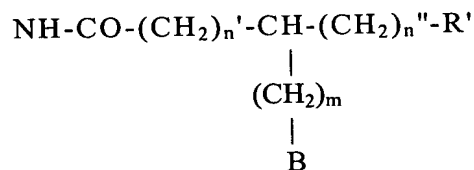
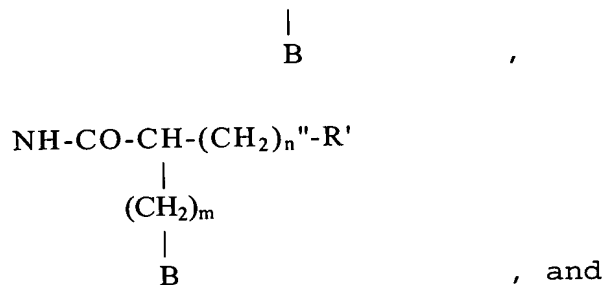
wherein

$i$  = degree of polymerization from 5 to 36,

$n$  = is an integer varying from 1 to 6,

wherein 50% to 100% of all R groups (corresponding to  $u$ ) are selected from the group consisting of





m = an integer varying from 1 to 6,

n' = an integer varying from 0 to 6,

n'' = an integer varying from 0 to 6,

B = a weak base,

R' represents NH<sub>3</sub><sup>+</sup> (corresponding to a number p);

or NH (corresponding to a number q) substituted by a structure selected from the group consisting of

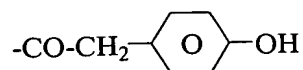
-CO-CH<sub>3</sub>,

-CO-(CHOH)<sub>r</sub>H

r being an integer from 1 to 15,

-CO-(CH<sub>2</sub>)<sub>s</sub>-(CHOH)<sub>r</sub>H

r being an integer from 1 to 15, and s being an integer from 1 to 6,



-SO<sub>2</sub>-Flu,



-CO-Flu, and

-CS-NH-Flu wherein

Flu is a fluorescent molecule;

and wherein 0% to 50% of all R groups (corresponding to f:  $0 < f \leq u$ ) are

$\text{NH}_3^+$  (corresponding to a number j); or

NH (corresponding to a number k), substituted by a structure selected from the group consisting of


-CO-CH<sub>3</sub>,

-CO-(CHOH)<sub>r</sub>H

r being an integer from 1 to 15,

-CO-(CH<sub>2</sub>)<sub>s</sub>-(CHOH)<sub>r</sub>H

r being an integer from 1 to 15, and s being an integer from 1 to 6,

-CO-CH<sub>2</sub>--OH  
-SO<sub>2</sub>-Flu,

-CO-Flu, and

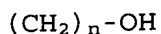
-CS-NH-Flu, wherein

Flu is a fluorescent molecule; or

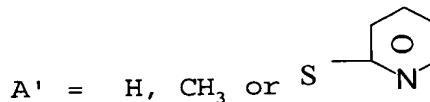
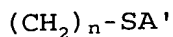
H (corresponding to a number h); or

(CH<sub>2</sub>)<sub>n</sub>H

n being an integer from 1 to 6 (corresponding to a number h); or



n being an integer from  
1 to 6 (corresponding to  
a number h); or



n being integer from 1  
to 6 (corresponding to a  
number h)

with  $i = u + j + k + h$

total number of  $\alpha \text{ NH}_3^+ = p = u - q$

total number of  $\omega \text{ NH}_3^+ = j = f - (k + h)$

total number of  $\text{NH}_3^+ = m = p + j + 1$

with the proviso that:

$$1) u \geq i/2$$

$$2) m \geq i/2.$$

27. (canceled)

28. (currently amended) A composition comprising  $[[\text{an}]]$   
at least one of the oligomeric ~~conjugate~~ conjugates according to  
claim 27, in association with an oligonucleotide.

29. (currently amended) A combined preparation, in  
the form of a kit-of-parts, comprising:

a)  $[[\text{an}]]$  the oligomeric conjugate according to claim  
20, and

b) an oligonucleotide for the simultaneous, separate  
or sequential use, for the *in vitro*, *in vivo*, or *ex vivo*

transfer of ~~[[said]]~~ a biological ~~molecules~~ molecule into a cytosol and/or cell nucleus.

30. (currently amended) A method for the *in vitro*, *ex vivo*, or *in vivo* intracellular transfer of oligonucleotides into a cytosol and/or in a cell nucleus of a cell, comprising:

treating said cell with ~~[[an]]~~ at least one of the oligomeric conjugate according to claim 20 in association with an oligonucleotide to transfer said oligonucleotide into the cytosol of said cell.

31. (currently amended) A method for the *in vitro*, *ex vivo*, or *in vivo* transfer of an oligonucleotide, into a cytosol and/or into a cell nucleus of a cell, comprising:

treating said cell with ~~[[an]]~~ at least one of the oligomeric conjugate according to claim 20 in association with said oligonucleotide to transfer said oligonucleotide into the cytosol of said cell.

32. (previously presented) The method according to claim 30, wherein the cells are selected from the group consisting of muscular, epithelial, endothelial, and myeloid cells.

33. (currently amended) A ~~pharmaceutical~~ composition, comprising as an active substance, ~~[[an]]~~ the oligomeric conjugate according to claim 20, in association with a ~~pharmaceutically~~ acceptable vehicle.

34. (previously presented) A kit or case comprising:

a) ~~[[an]]~~ the oligomeric conjugate according to claim 20,

b) at least one biological molecule to transfer, and

c) reagents enabling transfer of at least one biological molecule into a cell.

35. (currently amended) ~~[[An]]~~ A positively charged oligomeric conjugate ~~positively charged~~, comprising:

an oligomer with a polymerization degree (PD) from 5 to 36, formed from monomeric components ~~having free  $\text{NH}_3^+$  and substituted  $\text{NH}_3^+$~~  comprising monomeric compounds having substituted  $\text{NH}_3^+$  and monomeric compounds having unsubstituted  $\text{NH}_3^+$ , wherein

a) ~~[[the]]~~ wherein free  $\text{NH}_3^+$  groups of said monomeric components are in a ratio of at least 50%, said ratio being determined by nuclear magnetic resonance, by protonable residues, said residues being protonated in a weak acid medium, said protonation leading to a destabilization of a cellular membrane, and

b) said protonable residues possess the following properties:

wherein said protonable residues contain a functional group enabling them to be linked to said oligomer,

~~said protonable residues are not recognized as a recognition signal recognized by a cellular membrane receptor,~~

wherein said protonable residues comprise at least one free  $\text{NH}_3^+$  group and selected from the group consisting of midazoles, quinalines, pterines, and pycnidines.

~~e) the free  $\text{NH}_3^+$  of said monomers can optionally be substituted by uncharged residues leading to a reduction of the number of positive charges in comparison to the same oligomer before substitution,~~

~~d) molecules constituting a recognition signal recognized by a membrane cellular receptor may also optionally be present~~

~~by substitution of some of the free  $\text{NH}_3^+$  of said monomers,~~

~~on some of the uncharged residues leading to a reduction of the number of charges,~~

~~on some of said protonable residues leading to a destabilization of a cellular membrane, or~~

~~by substitution of a free  $\text{NH}_3^+$  of said protonable residues leading to a destabilization of a cellular membrane.~~